

TENT COOPERATION TREA

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

VAN HEUVEL, Margaretha
DSM N.V.
DSM Patents & Trademarks, Office
Delft
(994-0760)
P.O. Box 1
NL-2600 MA Delft
PAYS-BAS

Date of mailing (day/month/year) 22 November 2000 (22.11.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference WO 02954	
International application No. PCT/EP00/02191	International filing date (day/month/year) 09 March 2000 (09.03.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent
<input type="checkbox"/> the common representative		
Name and Address DSM N.V. Het Overloon 1 NL-6411 TE Heerlen Netherlands	State of Nationality NL	State of Residence NL
	Telephone No. +31 (0)455788111	
	Facsimile No. +31 (0)455719753	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input checked="" type="checkbox"/> the person	<input checked="" type="checkbox"/> the name	<input checked="" type="checkbox"/> the address
<input type="checkbox"/> the nationality		
<input type="checkbox"/> the residence		
Name and Address COSMOFORM B.V. Wateringseweg 1 NL-2611 XT Delft Netherlands	State of Nationality NL	State of Residence NL
	Telephone No. +31 (0)455788111	
	Facsimile No. +31 (0)455719753	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Dominique DELMAS
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

TENT COOPERATION TRE. Y

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

GEVERS & VANDER HAEGHEN N.V.
Livornostraat 7
B-1060 Brussel
P.O. Box 1
BELGIQUE

Date of mailing (day/month/year) 22 January 2001 (22.01.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference WO 02954	
International application No. PCT/EP00/02191	International filing date (day/month/year) 09 March 2000 (09.03.00)

1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address

 VAN HEUVEL, Margaretha
 DSM N.V.
 DSM Patents & Trademarks, Office
 Delft
 (994-0760)
 P.O. Box 1
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Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☐ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

 GEVERS & VANDER HAEGHEN N.V.
 Livornostraat 7
 B-1060 Brussel
 P.O. Box 1
 Belgium

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input checked="" type="checkbox"/> other: Former Agent

 The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

R. Raissi

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 07 November 2000 (07.11.00)	Applicant's or agent's file reference WO 02954
International application No. PCT/EP00/02191	Priority date (day/month/year) 09 March 1999 (09.03.99)
International filing date (day/month/year) 09 March 2000 (09.03.00)	
Applicant STREEKSTRA, Hugo et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
06 October 2000 (06.10.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer S. Mafla
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference WO 02954		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/02191	International filing date (day/month/year) 09/03/2000	Priority date (day/month/year) 09/03/1999	
International Patent Classification (IPC) or national classification and IPC C07C215/24			
Applicant COSMOFERM B.V. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 06/10/2000	Date of completion of this report 16.03.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Slootweg, A Telephone No. +49 89 2399 8326 

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05/09 01 MI 13:14 FAX +49 201 7531044

GOLDSCHEIDER A.G.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

GEVERS & VANDER HAEGHEN N.V.

Livornostraat

P.O. Box 1

B-1060 Brussel

BELGIQUE

19-03-2001 PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year)

16.03.2001

Applicant's or agent's file reference

WO 02954

IMPORTANT NOTIFICATION

International application No.

PCT/EP00/02191

International filing date (day/month/year)

09/03/2000

Priority date (day/month/year)

09/03/1999

Applicant

COSMOFERM B.V. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA



European Patent Office

D-80293 Munich

Tel. +49 89 2359-0 Tx: 523658 epmu d

Fax: +49 89 2359-4485

Authorized officer

Pfitzner, G

Tel. +49 89 2399-8032



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/02191

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-13 as originally filed

Claims, No.:

1-12 as originally filed

Drawings, sheets:

1/7-7/7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/02191

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 4,7
	No: Claims 1-3, 5-6, 8-12

Inventive step (IS)	Yes: Claims
	No: Claims 1-12

Industrial applicability (IA)	Yes: Claims 1-12
	No: Claims

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

R Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. D1 = EP-A-0 373 038
D2 = A. KISIC ET AL.: 'Studies in the sphingolipids series, XXXIL. Synthesis and resolution into optical antipods of C20-phytosphingosine' CHEM. PHYS. LIPIDS (1971), 7, p. 135-143 , 1972,
D3 = D. SHAPIRO ET AL. : 'The total synthesis of sphingosine' J. Am. Chem. Soc., vol. 80, 1952, p. 1194-1197,
D4 = ABRAHAMSSON, SIXTEN ET AL: 'Molecular arrangements in glycosphingolipids' CHEM. PHYS. LIPIDS (1972), 8(2), 152-79 , 1972,
D5 = STICHT, G. ET AL: 'Chemical synthesis of D,L-3-dehydrosphinganine, its C14-, C16-, and C20-homologs and the resolution into the enantiomeric forms' CHEM. PHYS. LIPIDS (1972), 8(1), 10-25 , 1972,
D6 = RUBINO, FEDERICO MARIA ET AL: 'Characterization of sphingosine long-chain bases by fast atom bombardment and high-energy collision- induced decomposition tandem mass spectrometry' ORG. MASS SPECTROM. (1992), 27(12), 1357-64, 1992,
D7 = US-A-5 723 497
D8 = WO-A- 93/20038
D9 = N.Z. STANACEV ET AL.: 'Studies on the chemistry of mucolipids: occurrence of the long-chain base icosisphingosine, composition of fatty acids, fractionation attempts' BIOCHIM. BIOPHYS. ACTA, vol. 98, 1965, pages 168-181,
D10 = WO-A-90/07571
D11 = GB-A-2 323 594
D12 = WO-A-98/49999 (cited in the application)
2. The following prior art documents disclose salts of "sphingoid bases" and their uses;
D1 (p. 12, l. 41; p. 13, l. 10; see also claim 1, l. 46; claims 49, 61 and 63),
D2 (salt of 8a with tartaric acid),
D3 (erythro-2-amino-3-hydroxy-4-octadecanoate-hydrochloride on p. 1196 right hand column),

D4 (compounds I, II and XI on p. 153, see also p. 154 "II. Materials and Methods", p. 156 "sphingosine hydrochloride and hydrobromide", and p. 159 first 3 lines),
D5 (p. 12 "3-hydro-sphingamine hydrochloride, p. 16, l. 16-24 and table 1),
D6 (compounds in fig. 1 on p. 1158),
D7 (for example compounds Ia-16, IIa-11, IIa-12, IIb-2, and IIc-8 together with claim 1)
D8 (the compounds disclosed on p. 6, l. 15-20 together with p. 6, l. 28-29, see claims 1-3 and p. 1, l. 20-23 and l. 33-37)
D9 (composition in Table I, and compounds indicated on p. 172, l. 8-10).
These compounds fall within the definition given in claims 1-3, 5, 6 and 8-12 (Art. 33 (2) PCT).

3. Claims 4 and 7 can be considered to satisfy Art. 33 (2) PCT because, sphingoid base salts of the specific acids indicated in claim 4 were not disclosed in the prior art and claim 7 because the use of ethanol or methyl isobutyl ketone as a solvent for preparing sphingoid base salts has not been disclosed in the prior art.
4. The sphingoid base derivatives of the prior art as set out above are also used for medicinal and cosmetic purposes. The problem to be solved can, therefore, be defined as finding further compounds for this purpose. The applicant has indicated on p. 2 that the claimed compounds have increased solubility in water and improved efficacy when formulated in aqueous compositions. Comparisons were made only with compositions containing pure base. No comparison has, therefore, been made to the closest prior art. As such claims 1-12 are considered not to satisfy Art. 33 (3) PCT.

Re Item VII

Certain defects in the international application

4. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-11 is not mentioned in the description, nor are these documents identified therein.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/02191

R Item VIII

Certain observations on the international application

5. The term "sphingoid" (resembling a sphingosine compound) is considered not clear (Art. 6 PCT).

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference WO 02954	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 00/ 02191	International filing date (day/month/year) 09/03/2000	(Earliest) Priority Date (day/month/year) 09/03/1999
Applicant DSM N.V. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/02191

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C215/24 A61K31/133 A61K7/48 A61K7/06 A61P31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, WPI Data, PAJ, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ABRAHAMSSON, SIXTEN ET AL: "Molecular arrangements in glycosphingolipids" CHEM. PHYS. LIPIDS (1972), 8(2), 152-79 , 1972, XP000920601 page 153; figure 1 page 156, paragraph B -page 159 page 158; figure 3 ---	1-3
X	WO 90 07571 A (UNIV EMORY) 12 July 1990 (1990-07-12) claims 20-27 ---	1-3, 10, 11
X	WO 93 20038 A (GIST BROCADES NV ;SMEETS JAN WILLEM HUBERT (NL); WEBER PIETER GIJS) 14 October 1993 (1993-10-14) page 10 -page 25 page 10, line 2 --- -/--	1-3



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

16 June 2000

Date of mailing of the international search report

06/07/2000

Name and mailing address of the ISA

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Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Pauwels, G

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 00/02191

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 373 038 A (FIDIA SPA) 13 June 1990 (1990-06-13) example 3 ---	1-3,6,8
X	STICHT, G. ET AL.: "Chemical synthesis of D,L-3-dehydrosphinganine, its C14-, C16-, and C20-homologs and the resolution into the enantiomeric forms" CHEM. PHYS. LIPIDS (1972), 8(1), 10-25 , 1972, XP000914283 page 18 ---	1-3
X	D. SHAPIRO ET AL. : "The total synthesis of sphingosine" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY., vol. 80, 1952, pages 1194-1197, XP002140009 DC US page 1196, last paragraph -page 1197, left-hand column ---	1-3,6
X	M. PROSTENIK ET AL.: "Studies in the sphingolipids series-XXIV Synthesis of C18-phytosphingosine" TETRAHEDRON., vol. 21, 1965, pages 651-655, XP002140010 OXFORD GB page 654, paragraph 4 page 655, paragraph 4 ---	1-3
A	US 5 723 497 A (IMOKAWA GENJI ET AL) 3 March 1998 (1998-03-03) claims ---	1-12
A	GB 2 323 594 A (MARTIN VICTOR ;KOKOTOS GEORGE (GR)) 30 September 1998 (1998-09-30) page 6 claim 3 ---	1-12
A	WO 98 49999 A (STREEKSTRA HUGO ;GIST BROCADES BV (NL); LAMBERS JOHANNES WILHELMUS) 12 November 1998 (1998-11-12) cited in the application claims ---	1-12
X	N.Z. STANACEV ET AL.: "Studies on the chemistry of mucolipids: occurrence of the long-chain base icosisphingosine, composition of fatty acids, fractionation attempts" BIOCHIM. BIOPHYS. ACTA, vol. 98, 1965, pages 168-181, XP000914314 page 172, paragraph 1 ---	1-3
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 00/02191

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	A. KISIC ET AL.: "Studies in the sphingolipids series, XXXIL. Synthesis and resolution into optical antipods of C20-phytosphingosine" CHEM. PHYS. LIPIDS (1971), 7, 135-143 , 1972, XP000914282 page 142 -page 143 -----	1-3
X	RUBINO, FEDERICO MARIA ET AL: "Characterization of sphingosine long-chain bases by fast atom bombardment and high-energy collision-induced decomposition tandem mass spectrometry" ORG. MASS SPECTROM. (1992), 27(12), 1357-64 , 1992, XP000914394 page 1337, right-hand column, paragraph 3 -----	1-3

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/02191

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9007571	A	12-07-1990	US 5190876 A AU 4816790 A CA 2006015 A GR 89100846 A US 5459057 A	02-03-1993 01-08-1990 27-06-1990 15-03-1991 17-10-1995
WO 9320038	A	14-10-1993	AT 147067 T AU 670818 B AU 4959093 A CA 2131184 A DE 69307131 D DE 69307131 T EP 0633875 A ES 2098735 T US 5631356 A	15-01-1997 01-08-1996 08-11-1993 14-10-1993 13-02-1997 24-04-1997 18-01-1995 01-05-1997 20-05-1997
EP 0373038	A	13-06-1990	IT 1235162 B AT 149506 T AU 632771 B AU 4566489 A CA 2004190 A DE 68927821 D DE 68927821 T DK 589789 A HU 209561 B HU 52107 A, B JP 2200691 A JP 3004297 B NO 894819 A NZ 231590 A US 5792858 A US 5519007 A	22-06-1992 15-03-1997 14-01-1993 21-06-1990 02-06-1990 10-04-1997 25-09-1997 03-06-1990 28-07-1994 28-06-1990 08-08-1990 31-01-2000 05-06-1990 23-12-1992 11-08-1998 21-05-1996
US 5723497	A	03-03-1998	JP 6271443 A JP 6271444 A JP 6271445 A JP 6271446 A JP 6271447 A JP 6271448 A JP 6271449 A JP 6321766 A JP 6321873 A JP 7017849 A DE 69419601 D DE 69419601 T EP 0691327 A WO 9421595 A	27-09-1994 27-09-1994 27-09-1994 27-09-1994 27-09-1994 27-09-1994 27-09-1994 22-11-1994 22-11-1994 20-01-1995 26-08-1999 02-12-1999 10-01-1996 29-09-1994
GB 2323594	A	30-09-1998	NONE	
WO 9849999	A	12-11-1998	EP 0914075 A	12-05-1999